Georg Marckmann, Sebastian Schleidgen
Institute for Ethics, History and Theory of Medicine

Personalized medicine and fair allocation of resources: Do we set the right priorities?

EACME Annual Conference

„Personalised Medicine“ – medicine for the person?
Ethical challenges for medical research and practice

Bochum, 19-21 September 2013

Personalized medicine – a „new“ paradigm?!

PM: field with (analytically) no clear boundary ⇨ object of inquiry??

Systematic literature search ⇨ 2457 articles with PM/IM in title/abstract ⇨ 683 articles with one or more definitions!

- analysis of components + quality criteria of definitions
- cf. Sebastian Schleidgens paper at 16:30 (sess. 5)

Definition:

PM seeks to improve stratification of health care by utilizing biological information and biomarkers on the level of molecular disease pathways, genetics, proteomics as well as metabolomics

De facto: patient subgroups ⇨ *stratified medicine*

Ethical implications of PM: Methods

Three methodological elements

(1) Literature review

(2) Analytic investigation

(3) Qualitative interview study with experts & stakeholders in the German hc system

Schleidgen and Marckmann *BMC Medical Ethics* 2013, **14**:20
http://www.biomedcentral.com/1472-6939/14/20

BMC Medical Ethics

RESEARCH ARTICLE Open Access

Re-focusing the ethical discourse on personalized medicine: a qualitative interview study with stakeholders in the German healthcare system

Sebastian Schleidgen* and Georg Marckmann

Ethical Implications of PM: Overview

		Areas of personalized medicine		
		Research	*Application*	
			Prediction/Prevention	Therapy
Ethical issues	individual level	• Informational self-determination • Confidentiality/ data protection • Informed consent for add-on-studies	• Informational self-determination • Data protection • Implication of predictive information for individual • Overemphasis of individual responsibility for health	• Higher risks due to insufficient testing • Implications for physician-patient relationship • (Confidentiality, data protection) • (Informational self-determination)
	societal level	• Allocation of research resources • Study design (patient relevant outcomes)	• Discrimination of „bad risks“ • (Access, distributive justice)	• Cost impact? => Access, distributive justice • (Discrimination of bad responders)

ORIGINALARBEIT

Alter Wein in neuen Schläuchen? Ethische Implikationen der Individualisierten Medizin

Sebastian Schleidgen · Georg Marckmann

Ethik Med (2013) 25:223–231
DOI 10.1007/s00481-013-0267-3

Personalized Medicine & Justice: Overview

Distributive justice: 4 levels

Level	Area	Explanation
1	**Allocation** of research resources	Allocation of resources *into* personalized medicine (vs. alternative ways to promote health, prevent and treat diseases)
2		Allocation of resources *within* the field of personalized medicine
3	**Distribution** of PM products	Distribution of / access to personalized medicine
4	**Indirect consequences**	Discrimination/disadvantages due to diagnostic & prognostic information from personalized medicine

Personalized Medicine & Justice: Overview

Distributive justice: 4 levels

Level	Area	Explanation
1	**Allocation** of research resources	Allocation of resources *into* personalized medicine (vs. alternative ways to promote health, prevent and treat diseases)
2		Allocation of resources *within* the field of personalized medicine
3	**Distribution** of PM products	Distribution of / access to personalized medicine
4	**Indirect consequences**	Discrimination/disadvantages due to diagnostic & prognostic information from personalized medicine

Allocation of research resources (1)

Level 1: Allocation of resources *into* PM (vs. other alternatives)

- Central issue: high public and private investment in PM ⇨ right priorities?
  - ⇨ Directed towards priority health needs of the population?
  - ⇨ Higher health gain if resources are invested in other approaches?
  - ⇨ Does it take into account existing inequalities in health status?

Policy options:

(1) Explicit priority setting in public funding for research
- Health care needs in an ageing society (chronic diseases, multi-morbidity)
- Priority for disadvantaged (sub-)populations
- Potential for improving health status in population
- Priority for common diseases?
- Cost-effectiveness (efficiency) – anticipative assessment possible?

(2) Incentives for pharmaceutical companies to invest in areas with high priority

Allocation of research resources (2)

Level 2: Resource allocation *within* PM

- Investment in profitable areas ⇨ populations with rare (genetic) profile are neglected ⇨ „orphan populations“
- Neglect of vulnerable, already disadvantaged subpopulations
- Research with patient subgroups beyond PM neglected ⇨ higher risks through insufficiently tested interventions

Policy options

- Incentives for investments by pharmaceutical industry in „orphan populations“ (cf. current orphan drug regulation)
- More public research funding in (genetically) rare patient populations
- Challenge: increasing number of „orphan drugs“ ⇨ increasing public spending necessary ⇨ limits? priorities?

Personalized Medicine & Justice: Overview

Distributive justice: 4 levels

Level	Area	Explanation
1	**Allocation** of research resources	Allocation of resources *into* personalized medicine (vs. alternative ways to promote health, prevent and treat diseases)
2		Allocation of resources *within* the field of personalized medicine
3	**Distribution** of PM products	Distribution of / access to personalized medicine
4	**Indirect consequences**	Discrimination/disadvantages due to diagnostic & prognostic information from personalized medicine

Distribution of personalized medicine (3)

Justice requires: General & equal access to personalized medicine

Central question: *Will health care become more or less expensive with PM?*

Optimistic scenario: *Cost savings* through targeted therapies with a higher effectiveness and less side effects

Pessimistic scenario: *cost increase* due to additional (biomarker) diagnostic, high costs for R&D and production of PM for small populations ("niche busters")

Cost increase ⇨ (potentially) limited access for less affluent patients with less comprehensive insurance coverage
⇨ Creation of new & aggravation of existing inequalities (on a national and global scale!)

Distribution of personalized medicine (3)

Cost-effectiveness depends on several factors:

- Size of target population
- Number & cost of biomarker tests (i.e. test strategy)
- Likelihood of modified treatment decision due to diagnostic
- Cost impact of modified treatment decision

⇨ Cost-effectiveness varies considerably! (Wong et al. 2010)

⇨ Individual assessment of C/E-ration for each PM intervention

⇨ *Shape* the cost-effectiveness of PM!

⇨ HNPCC-screening: between 20.000€ and 1.500.000€/LYS depending on test strategy! (Mayer & Rogowski 2011)

Challenge (e.g. in oncology):

- Small incremental benefit ⇨ bad cost-effectiveness (HER-2 & Trastuzumab: $125.000/QALY [Elkin et al. 2004])

⇨ Does the (small) additional benefit (at the end of life) justify the high costs?

Distribution of personalized medicine (3)

Cost-benefit-assessment requires valid *benefit* assessment!

At the time of licensing of the drug: benefit under routine conditions difficult to assess

- Studies for licensing: usually assess efficacy under ideal conditions
- Selected, not representative samples
- Surrogate endpoints instead of patient relevant endpoints (⇨ overall survival, quality of life)
- No head-to-head comparison with standard treatment
- Incomplete data transparency (reporting & publication bias)

⇨ Requirements for a needs oriented and fair allocation & distribution are often not met!

Distribution of personalized medicine (3)

Policy options

(1) First: Improve benefit assessment

- Independent, publicly financed clinical studies after licensing of the drug (patient relevant outcomes)
- (Initially) coverage only in clinical studies („coverage with evidence development“)
- (Germany: benefit assessment according to AMNOG too early!)

(2) Then: Cost-benefit assessment (CEA/CUA)

- Price negotiations with pharmaceutical industry
- Limited of coverage of interventions with bad incremental C/E-ratio
- Goal: unlimited access to *real innovations* for all patients, exclusion of „pseudo innovations“

Problem in Germany (& other countries): so far no open socio-political discourse on setting limits fairly in the hc system!

Finally...

I would like to thank

- *you* for your attention
- *my colleagues* in the BMBF-collaborative research project for their input
  - Sebastian Schleidgen (ethics)
  - Elisabeth Meyer/Wolf Rogowski (economics)
  - Simone von Hardenberg/Nikola Wilman (law)

Further Information: www.igv-ethik.de

Slides: www.dermedizinethiker.de

Contact: marckmann@lmu.de

Personalized Medicine & Justice: Overview

Distributive justice: 4 levels

Level	Area	Explanation
1	**Allocation** of research resources	Allocation of resources *into* personalized medicine (vs. alternative ways to promote health, prevent and treat diseases)
2		Allocation of resources *within* the field of personalized medicine
3	**Distribution** of PM products	Distribution of / access to personalized medicine
4	**Indirect consequences**	Discrimination/disadvantages due to diagnostic & prognostic information from personalized medicine

Indirect consequences (level 4)

Discrimination of patient subgroups through *secondary* information of PM about

- risk of disease, prognosis, treatment effectiveness
- Categorization: „good responder“ ⇔ „non-responder“, „difficult to treat“

Fairness implications:

- ➪ Restricted access to health care interventions
- ➪ Restricted access to health insurances or higher premiums
- ➪ Disadvantages in other areas (e.g. employment)
- ➪ Stigmatization of subpopulations

Policy options

- ➪ Restrictive regulation of access to sensitive (genetic) information (e.g. only physician & patient, patient controls access)
- ➪ Informed consent for testing: Information about (indirect) risks

Conclusion

Personalized medicine has (potentially) ethical implications

- ➪ most are not specific for PM
- ➪ depend on application of individualized strategies

Individualized prediction & prevention: mainly challenges on the individual level (excess diagnostic information!)

Individualized treatment: mainly challenges on societal level

- Allocation of research resources into/within PM
- Distribution of PM interventions (cost-effectiveness!)

No general rejection of PM, but

(1) „Monitoring“ of ethical implications

(2) Implement policies to ensure ethically acceptable development and application of PM

➪ *Shape* the development in the field of PM!